

Replacement Sheet

ntagonists

rgos PGYRYLFACSP-LTRLRCQRKQPCKLFTVVRKRQEFELDEVNINSLGCPK-- GHRCPSHHTQSG-

gonists

in-3 IEKLKEAKCKD-- YCHHHNATCHVEVIFRED-- RVSAAVVPSCCPQGWEGTRCDRHVQAF-

sin	DRSASGIPCN--FD-YCFHNNGTCRMIDP <u>DIN</u> --EVY-CRCPTEYFGNRCE <u>N</u> KPDSR-	D. melanogaster
urken	ETEIQMLPC <u>S</u> EA <u>Y</u> NTSF <u>C</u> LNGGH <u>C</u> FQHPMVNN--TVFHS <u>C</u> LCVND <u>D</u> <u>G</u> ERCAYKSWN <u>G</u> -	D. melanogaster
zitz	NITFP <u>T</u> YK <u>C</u> PETFD <u>A</u> W <u>C</u> LND <u>A</u> HCFAV <u>K</u> IADL--PVYS-CECAIGFM <u>G</u> OR <u>C</u> EY <u>K</u> I <u>D</u> NT-	D. melanogaster
zren	NVT <u>F</u> P <u>I</u> FACE <u>P</u> PTTYVA <u>W</u> Y <u>C</u> LND <u>G</u> T <u>C</u> FTVKHNE--ILYN-CE <u>C</u> ALGF <u>M</u> <u>G</u> PR <u>C</u> EY <u>K</u> I <u>D</u> GS-	D. melanogaster
α 1	TGTSHLV <u>K</u> CAE <u>E</u> KE <u>K</u> T-FCVNGGEC <u>F</u> MVKDLS-----NPSRYLCKCQPGFT <u>G</u> AR <u>C</u> TENPMKV-	Homo sapiens
α 1	TGTSHLV <u>K</u> CAE <u>E</u> KE <u>K</u> T-FCVNGGEC <u>F</u> MVKDLS-----NPSRYLCKCOPNE <u>F</u> IT <u>G</u> DRCON <u>Y</u> VMASF-	Homo sapiens
α 2	SWSGHARK <u>C</u> NETAKS-Y <u>C</u> VNGGG <u>C</u> YY <u>I</u> EGIN-----QLS--CKCPNGFF <u>G</u> QRC <u>C</u> LE <u>K</u> PLRL-	Homo sapiens
α 2	SWSGHARK <u>C</u> NETAKS-Y <u>C</u> VNGGG <u>C</u> YY <u>I</u> EGIN-----QLS--CKCPVGYT <u>G</u> DR <u>C</u> QQFAMVN <u>F</u> -	Homo sapiens
α 3	ERSHEFKP <u>C</u> RDKDLA-Y <u>C</u> LND <u>G</u> EC <u>F</u> VIE <u>L</u> TG-----SHK-HCR <u>C</u> REG <u>Y</u> <u>Q</u> <u>G</u> <u>V</u> RC <u>D</u> Q-FLPKTD	Homo sapiens
α 4	MPTDHEEP <u>C</u> GPSHK <u>S</u> -F <u>C</u> LNG <u>G</u> <u>L</u> <u>C</u> YY <u>V</u> PTIP-----SP--FCR <u>C</u> VENYT <u>G</u> AR <u>C</u> EE <u>V</u> FLPGS-	Homo sapiens
β F	SVRNSDSEC <u>P</u> LSHDG-Y <u>C</u> LHDG <u>V</u> CMYIE <u>A</u> LD-----KYA-CNCWVG <u>Y</u> <u>I</u> <u>G</u> ERC <u>Q</u> YRD <u>L</u> KWW-	Homo sapiens
β F_alpha	AVVSHFNDCPDSHTQ-F <u>C</u> FH-GT <u>C</u> RF <u>L</u> VQED-----KPA-CVCHSG <u>V</u> <u>V</u> <u>G</u> AR <u>C</u> E <u>H</u> ADLLAV-	Homo sapiens
stacellulin	KRKGHFSR <u>C</u> P <u>Q</u> YKH-Y <u>C</u> IK-G <u>C</u> RF <u>V</u> V <u>A</u> EQ-----TPS-CVC <u>D</u> E <u>G</u> <u>I</u> <u>G</u> ARC <u>C</u> ER <u>V</u> D <u>L</u> F <u>Y</u> L-	Homo sapiens
aphiregulin	RNRKKKNP <u>C</u> NAEF <u>Q</u> N-F <u>C</u> I <u>H</u> -GE <u>C</u> KK <u>I</u> E <u>H</u> LE-----AVT-CKC <u>Q</u> E <u>Y</u> <u>F</u> GER <u>C</u> EKSMKTH-	Homo sapiens
β -EGF	GLGKKRDP <u>C</u> LR <u>K</u> YKD-F <u>C</u> I <u>H</u> -GE <u>C</u> KK <u>V</u> K <u>E</u> LR-----APS-CICH <u>P</u> <u>G</u> <u>Y</u> <u>H</u> GER <u>C</u> H <u>G</u> LSLP <u>V</u> E-	Homo sapiens
coregulin	VAQVSI <u>T</u> <u>K</u> <u>C</u> SSDMNG-Y <u>C</u> LH-G <u>C</u> I <u>Y</u> <u>L</u> VDMS-----QNY-CR <u>C</u> EV <u>G</u> <u>Y</u> <u>T</u> <u>G</u> VR <u>C</u> E <u>H</u> FF <u>L</u> TV <u>H</u> -	Homo sapiens
digen	VALKF <u>S</u> HP <u>C</u> LEDHNS-Y <u>C</u> IN-G <u>A</u> <u>C</u> <u>A</u> F <u>H</u> HE <u>L</u> K-----QAI-CR <u>C</u> FT <u>G</u> <u>T</u> <u>I</u> <u>G</u> <u>R</u> CE <u>H</u> ILTTS <u>Y</u> -	Mus musculus

onserved cysteine #: 1

2

3

4

5

6

FIGURE 1

Replacement Sheet

FIGURE 2

Replacement Sheet

FIGURE 3

Replacement Sheet

HUMAN			Sequence ID #
NRG1_alpha	<----- Exon A -----><----- Exon B ----->		
TGTSHLVKCAEKEKTF <u>CVNNGECFMVKDLSNPSRYLCKCOPGFTGARCTENVPMKVQ...</u>	14	
NRG1_betaTGTSHLVK <u>CAEKEKTF</u> <u>CVNNGECFMVKDLSNPSRYLCKCPNEFTGDR<u>CQNTYMASFY...</u></u>	15	
Translated genomic locusTGTSHLVK <u>CAEKEKTF</u> <u>CVNNGECFMVKDLSNPSRYLCK*</u>	73 , 128	
NRG2_alphaSWSGHARK <u>CNETAKSYCVNNGCYYIEGINQLS--CKCPNGFFGQRCL</u> EKLPLRLY...	16	
NRG2_betaSWSGHARK <u>CNETAKSYCVNNGCYYIEGINQLS--CKCPVGYTGDR</u> CQQFAMVNFY...	17	
Translated genomic locusSWSGHARK <u>CNETAKSYCVNNGCYYIEGINQLS--CK*</u>	74 , 129	
NRG3ERSEHFKP <u>CRDKDIALAYCLNDGE</u> CFVIETLTGSH-KHCRCKEGQGV <u>RCDQ</u> -FLPKTD...	18	
Translated genomic locusERSEHFKP <u>CRDKDIALAYCLNDGE</u> CFVIETLTGSH-KH <u>R*</u>	75 , 130	
NRG4MPTDHEEP <u>CGPSHKSFCLNGGLCYVIPTIPSPF--CRCV</u> ENTGAR <u>CEEVFLPGSS</u> ...	19	
Translated genomic locusMPTDHEEP <u>CGPSHKSFCLNGGLCYVIPTIPSPF--CR*</u>	76 , 131	
EGFSVRNSDSE <u>CPLSHDGYCCLHDGGVCMYIEALDKYA--CNCVVG</u> YIGER <u>CQYRDLKWW</u> ...	20	
Translated genomic locusSVRNSDSE <u>CPLSHDGYCCLHDGGVCMYIEALDKYA--CK*</u>	77 , 132	
TGF_alphaAVVSHFND <u>CPDSHTQFCFH-GTCRFLVQEDKPA--CVCHSGVGVGARCEHADLLAVV</u> ...	21	
Translated genomic locusAVVSHFND <u>CPDSHTQFCFH-GTCRFLVQEDKPA--CV*</u>	78 , 133	
BetacellulinKRKGHF <u>SRCPKQYKHYCIK-GRCRFVVAEQTPS--CVCDEGGYI</u> GARCE <u>RVDLFYL</u> R...	22	
Translated genomic locusKRKGHF <u>SRCPKQYKHYCIK-GRCRFVVAEQTPS--CV*</u>	79 , 134	

FIGURE 4A

Replacement Sheet

Amphiregulin Translated genomic locus	...RNRKKKKNP <u>CNAE</u> FQN <u>FCI</u> H-GE <u>CKYIEHLEAVT</u> -- <u>CKCQQEYFGERCGEKS</u> MKTHS... ...RNRKKKKNP <u>CNAE</u> FQN <u>FCI</u> H-GE <u>CKYIEHLEAVT</u> -- <u>CK*</u>	23 80, 135
HB-EGF Translated genomic locus	...GLGKKRDP <u>CLRKYKDF</u> <u>CIH</u> -GE <u>CKYVKEILRAPS</u> -- <u>CI</u> <u>CHPGYHGERCHG</u> LSPVEN... ...GLGKKRDP <u>CLRKYKDF</u> <u>CIH</u> -GE <u>CKYVKEILRAPS</u> -- <u>CM*</u>	24 81, 136
Epiregulin Translated genomic locus	...VAQVSI <u>TKCSSDMNGY</u> <u>CLH</u> -G <u>Q</u> <u>Q</u> <u>CITYLV</u> DMSQNY-- <u>CRCEVGGYT</u> GVR <u>CEHFFFLTVHQ</u>VAQVSI <u>TKCSSDMNGY</u> <u>CLH</u> -G <u>Q</u> <u>Q</u> <u>CITYLV</u> DMSQNY-- <u>CR*</u>	25 82, 137
Epigen (Mouse) Trans. mouse genomic locus Trans. mouse genomic locus	...VALKFSS <u>HPCLEDHN</u> SYC <u>IN</u> -G <u>A</u> <u>CAFHH</u> E <u>LKQAI</u> -- <u>CRCF</u> T <u>GYT</u> G <u>QRCEH</u> L <u>LT</u> SYA... ...VALKFSS <u>HPCLEDHN</u> SYC <u>IN</u> -G <u>A</u> <u>CAFHH</u> E <u>LKQAI</u> -- <u>CR*</u> ...VALKFSS <u>HPCLEDHN</u> SYC <u>IN</u> -G <u>A</u> <u>CAFHH</u> E <u>LEKAI</u> -- <u>CR*</u>	26 83, 138 84, 139

FIGURE 4B

Replacement Sheet

i) TGF alpha Sequence ID #
EGF DOMAIN NUMBER -----SEQUENCE-----
1. EGF_47_82* CPDSHTQFCF-HGT-CRFLVQEDKPACVCHSG--YVGAR--C 72

ii) EPIDERMAL GROWTH FACTOR Sequence ID #
EGF DOMAIN NUMBER -----SEQUENCE-----
1. EGF_318_354 CKLR-KGNCS--STVCGQDL--QSHLCMCAEGYALS RDRKYC 27
2. EGF_360_395 CAFW-NHGC--TLGCKNTP--GSYYCTCPVGFVLLPDGKRC 28
3. EGF_401_436 CPRN-VSEC--SHDCVLTS--EGPLCFCP EGSVLERDGKTC 29
4. EGF_439_476 CSSPDNGGCS--QLCVPLSP--VSWECD CFPGYDLQLDEKSC 30
5. EGF_745_780 CLYQ-NGGC--EHICKKRL--GTAWCSCREGFMKASDGKTC 31
6. EGF_835_868 CAPV---GCS-MYARCISEG--EDATCQCLKG--FAGDGKLC 32
7. EGF_874_910 CEMG-VPVCPPASSKCINTE--GGYVCRCSEG--YQGDGIHC 33
8. EGF_916_951 CQLG-VHSCGENAS-CTNTE--GGYTCMCAGR--LSEPGЛИC 34
9. EGF_976_1012* CPLSHDGYCL-HDGVCMYIEALDKYACNCVVG--YIGER--C 35

FIGURE 5B

New Sheet

iii) Notch1

EGF DOMAIN NUMBER	SEQUENCE	Sequence ID #
1. EGF_24_57	CSQ-----PGETCLNGGKCEAANGTE-----ACVCG-GAFVGPRC	36
2. EGF_63_98	CLS-----TPCKNAGTCH-VVDRRGVADYACSCA-LGFSGPLC	37
3. EGF_106_138	CLT-----NPCRNGGTCD-LLTLT---EYKCRCP-PGWSGKSC	38
4. EGF_144_175	CAS-----NPCANGGQC---LP-FEASYICHCP-PSFHGPTC	39
5. EGF_182_215	CGQ-----KPRLCRHGGTCHNEVGSY----RCVCR-ATHTPN	40
6. EGF_222_254	CSPSP-----CQNGGTCRPTGDV---THECACL-PGFTGQNC	41
7. EGF_261_292	CPGN-----CKNGGACV-DGVN---TYNCPCP-PEWTGQYC	42
8. EGF_299_332	CQL-----MPNACQNGGTCHNTHGGY---NCVCV-NGWTGEDC	43
9. EGF_339_370	CAS-----AACFHGATCH-DRVA---SFYCECP-HGRTGLLC	44
10. EGF_376_409	CIS-----NPCNEGNSCD-TNPV--NGKAICTCP-SGYTGpac	45
11. EGF_416_449	CSL-----GANPCEHAGKCINTLGSF---ECQCL-QGYTGPRC	46
12. EGF_456_487	CVS-----NPCQNDATCL-DQIG---EFQCMCM-PGYEGVHC	47
13. EGF_494_525	CAS-----SPCLHNGRCL-DKIN---EFQCECP-TGFTGHLC	48
14. EGF_532_563	CAS-----TPCKNGAKCL-DGPN---TYTCVCT-EGYTGTHC	49
15. EGF_570_600	CDPDP-----CHYG-SCK-DGVA---TFTCLCR-PGYTGHHC	50
16. EGF_607_638	CSS-----QPCRLRGTCQ-DPDN---AYLCFCL-KGTTGPNC	51
17. EGF_645_675	CAS-----SPC-DSGTCL-DKID---GYECACE-PGYTGSMC	52
18. EGF_682_713	CAG-----NPCHNGGTC---ED-GINGFTCRCP-EGYHDPTC	53
19. EGF_720_750	CNS-----NPCVHGACRD---SLN---GYKCDCD-PGWSGTNC	54
20. EGF_757_788	CES-----NPCVNGGTCK-D-MTS---GIVCTCR-EGFSGPNC	55
21. EGF_795_826	CAS-----NPCLNKGTC---IDD---VAGYKCNCL-LPYTGATC	56
22. EGF_833_867	CAP-----SPCRNGGEGR-QSED-YES-FSCVCPTAGAKGQTC	57
23. EGF_874_905	CVL-----SPCRHGASCQ-NTHG---XYRCHCQ-AGYSGRNC	58
24. EGF_912_943	CRPNP-----CHNGGSCT-DGIN---TAFCDCL-PGFRGTFC	59
25. EGF_950_981	CAS--DP-----CRNGANCT-DCVD---SYTCTCP-AGFSGIHC	60
26. EGF_988_1019	CTESS-----CFNGGTCV-DGIN---SFTCLCP-PGFTGSYC	61
27. EGF_1026_1057	CDS-----RPCILLGGTCQ-DG---RGLHRCTCP-QGYTGPN	62
28. EGF_1064_1095	CDS-----SPCKNGGKCW-QT---HTQYRCECP-SGWTGLYC	63
29. EGF_1102_1143	CEVAAQRQGVDVARLCQHGGLCV-DAGN---THHCRCQ-AGYTGSYC	64
30. EGF_1150_1181	CSP-----SPCQNGATCT-DYLG---GYSCKCV-AGYHGVNC	65
31. EGF_1188_1219	CLS-----HPCQNGGTCL-DLPN---TYKCSCP-RGTQGVHC	66
32. EGF_1226_1265	CNPPVDPVSRS--PKCFNNGTCV-DQVG---GYSCTCP-PGFVGERC	67
33. EGF_1272_1305	CLS-----NP_CDARGTQN-CVQR--VNDFHCECR-AGHTGRRC	68
34. EGF_1312_1346	CKG-----KPCKNGGTCA-VASN-TARGFICKCP-AGFEGATC	69
35. EGF_1353_1384	C-----GSLRCLNGGTCISGPRSP---TCLCL-GPFTGPEC	70
36. EGF_1392_1426	CL-----GGNPCYNQGTCEPTSESPF---YRCLCP-AKFNGLLC	71

FIGURE 5C

Replacement Sheet

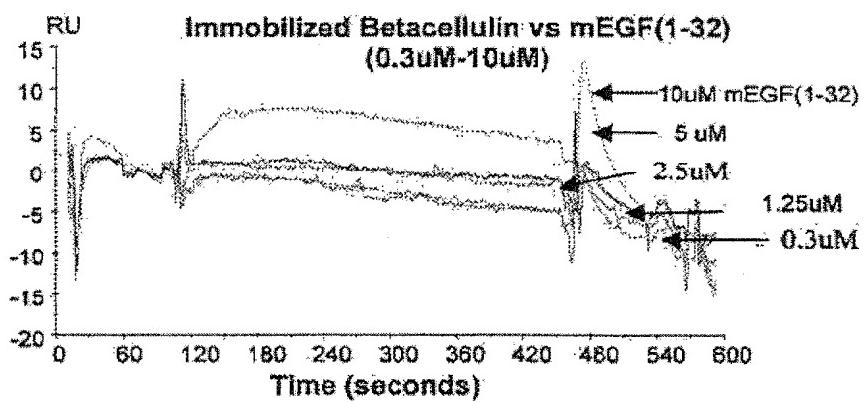


FIGURE 6A

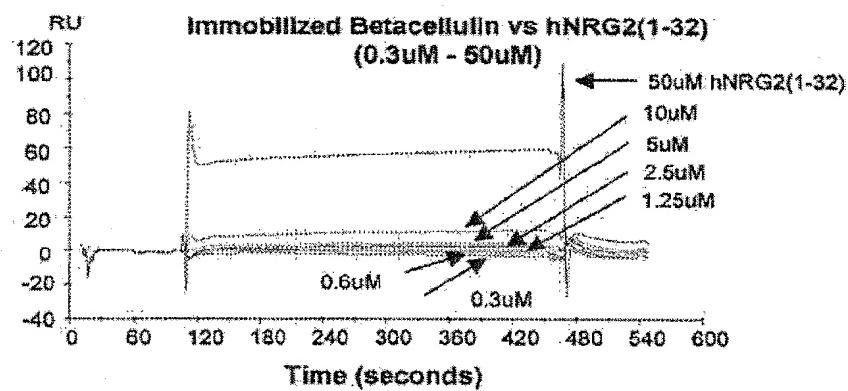


FIGURE 6B